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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,676	06/01/2001	Takashi Miki	Q64808	7681

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EXAMINER
TUCKER, ZACHARY C

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 06/20/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,676	MIKI ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,9-15 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 6, 9-15, and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *part of #13*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

The amendment filed 02 May 2003 (paper #13), the supplemental amendment filed 03 June 2003 (paper #14) and the second supplemental amendment filed 04 June 2003 (paper #15) have been entered.

Status of Previous Claim Rejections - 35 USC § 102

Prior to setting forth the outstanding prior art rejections in the instant case, for the sake of clarity, the references previously cited in the case and the name by which the reference is referred to in this Office action are listed:

Urbanski et al, Polish Journal of Chemistry, vol. 58, pages 1227-1229 (1984). "Urbanski et al"

Ramage et al, "A Kinetic Study of Phosphinic Carboxylic Mixed Anhydrides" J. Chem. Soc. Perkin Trans. I, pages 1617-1622 (1985). "Ramage et al"

US patent 4,874,558 (Fife et al) "Fife et al"

Benoiton et al, "Preparation of activated esters of N-alkoxycarbonylamino and other acids by modification of the mixed anhydride procedure" J. Peptide Protein Res. vol. 42, pages 278-283 (1993). "Benoiton et al"

Gaede, B., Organic Process Research and Development, vol. 3, pages 92-93 (1999). "Gaede"

Claims 1, 5, 9-13 and 17 remain rejected under 35 U.S.C. 102(b), as being anticipated by Urbanski et al, for reasons of record in the Office action dated 14 March 2003 (paper #11), and further for reasons given in the next paragraph and hereinbelow in the section headed "Response to Arguments."

Urbanski et al discloses on page 1229, in both "Stage 1" and "Stage 2," a method according to claims 1, 5, 9-13 and 17 for making unsymmetrical carboxylic anhydrides by adding together a mixture of carboxylic acid and organic base and a solution of carboxylic acid activating agent, said carboxylic acid activating agent being either a

sulfonic acid chloride in "Stage 1" or a mixed carboxylic-sulfonic acid anhydride in "Stage 2."

Claims 1, 5 and 11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Gaede, for reasons of record in the Office action dated 14 March 2003 (paper #11), and further for reasons given in the next paragraph and hereinbelow in the section headed "Response to Arguments."

Gaede discloses a method according to claims 1, 5 and 11 (and claim 9 – see "New Claim Rejections – 35 U.S.C. 102") for making mixed carboxylic-phosphoric anhydrides by adding together a carboxylic acid and organic base and the carboxylic acid activating agent diethyl chlorophosphate.

Claims 1, 5, 9 and 11 remain rejected under 35 U.S.C. 102(b) as being anticipated by Fife et al, for reasons of record in the Office action dated 14 March 2003 (paper #11), and further for reasons given in the next paragraph and hereinbelow in the section headed "Response to Arguments."

Fife et al discloses the method of claims 1, 5, 9 and 11 in Example 1 and Table 1. All three elements, carboxylic acid, carboxylic acid activating agent, and organic base are combined simultaneously.

Claims 1, 5, 6, 9-15 and 17-19 remain rejected under 35 U.S.C. 102(b), as being anticipated by Benoiton et al, for reasons of record in the Office action dated 14 March

2003 (paper #11), and further for reasons given in the next paragraph and hereinbelow in the section headed "Response to Arguments."

Benoiton et al discloses a method according to claims 1, 5, 6, 9-15 and 17-19 for making mixed anhydrides from N-protected amino acids and chloroformates, wherein N-methyl morpholine is the organic base employed on pages 279-280. The chloroformate, amino acid and N-methyl morpholine are all added together in the method disclosed by Benoiton et al.

Claims 1, 5, 6, 9-15 and 17-19 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ramage et al, for reasons of record in the Office action of 14 March 2003, paper #11, and further for reasons given in the next paragraph and hereinbelow in the section headed "Response to Arguments."

Ramage et al discloses adding together in equimolar amounts an amino acid and N-methylmorpholine and a phosphinic acid chloride, to make a mixed anhydride (page 1617).

New Claim Rejections - 35 USC § 102

New claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Urbanski et al. Urbanski et al discloses simultaneous addition of carboxylic acid and organic base to the carboxylic acid activating agent. Limitations of new claim 21 are disclosed in Table 2, and in "Scheme 2" on page 1229.

Claim 9 and new claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaede. The diethyl chlorophosphate reagent employed by Gaede is an acid chloride of phosphoric acid (the rejection of claim 9 as being anticipated by Gaede should have been included with the rejections based on that reference in the previous Office action, dated 14 March 2003 – paper #11). Gaede discloses simultaneous addition of organic base and carboxylic acid, and the substituents "R" in Table 1 on page 93 of Gaede meet the limitations in claim 21.

New claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Fife et al. Fife et al discloses simultaneous addition of carboxylic acid and organic base, and the substituents specified in claim 21 are disclosed in Example 1 and Table 1 of the Fife et al patent.

New claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Benoiton et al. The limitations of claims 21 and 22 are disclosed on pages 279-280.

New claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Ramage et al. The limitations of claims 21 and 22 are disclosed on page 1617 of Ramage et al. The organic base and carboxylic acid are added simultaneously.

Claims 1, 5, 6, 9-13, 15, 17-19, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by US 3,264,281 (Applewhite et al).

Applewhite et al discloses the method of claims 1, 5, 6, 9-15, 17-19, 21 and 22, for instance, in Example V, wherein as the first step in the synthesis of N-carbobenzoxyglycinanilide, the mixed anhydride ethyl N-benzyloxycarbonylglycine carbonate is formed. The carboxylic acid activating agent is ethyl chloroformate and the carboxylic acid is an N-protected amino acid. The organic base is triethylamine. All three reagents are employed in equimolar amounts.

Column 4, lines 53-75 and on to column 5, lines 1-8 explain that though the end product of the syntheses disclosed in that patent are amides, the intermediate is a carboxylic-carbonic mixed anhydride.

New Claim Rejections - 35 USC § 112

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The definition of R^2 in claim 20 includes the recitation, "provided that said amino, mercapto, guanidyl, carboxyl, hydroxy and imidazolyl groups which may be present in R^2 and substituent groups contained therein are in a protected form." There is no antecedent basis for the aforementioned functional groups in R^2. Claim 20 has been examined on the merits in this Office action as though the aforementioned phrase were absent from the claim.

Response to Arguments

Applicant's argument in response to the rejections based on Urbanski et al, Gaede, Fife et al, and Benoiton et al are two-fold.

1. That none of the previously cited references disclose the addition of a solution of carboxylic acid and organic based to a carboxylic acid activating agent to make a mixed anhydride.

2. That the alleged unexpected results demonstrated in the instant specification's Examples rebuts the rejections under 35 U.S.C. 102(b).

First, point #1 is addressed:

Out the outset, Applicant's attention is directed to page 1229 of the Urbanski et al reference, "Stage 2," in which the two solutions are mixed in a different order than in "Stage 1." All of the references *do not* disclose the same order of addition of reagents to the reaction mixture.

The issue of the literal meaning of the word "add" must be addressed. Webster's II New Riverside University Dictionary, on page 77, defines the word "add" as *'1. To unite or join so as to increase in size, quantity, or scope.'* or, alternatively, *'2. To combine (e.g., a column of figures) to form a sum.'*

In the second definition of "add," the addition of a column of figurers is given only as an example. The definition of the word "sum," which appears in the same dictionary on page 1160: *'1. The total obtained as a result of adding. 2. The whole amount, quantity or number'* makes it abundantly clear that the word "sum," as it is referred to in the definition of the word "add," is not limited in meaning to only mathematics.

From the definition thereof, it can be seen that the word "add" is synonymous with combine, join or unite, and that therefore, "adding" is synonymous with "combining," "joining" or "uniting," which are the present participle forms of the verbs.

The word "add," when present in a claim describing a method, does not presuppose any particular order of addition. The literal meaning of "add" only has significance when one looks at the combination produced by the adding. Only then it can it be determined exactly what has been added to what.

A test that is sometimes used for determining whether an invention is anticipated or not that is the infringement test. Practitioners of the methods disclosed in the Urbanski et al, Ramage et al, Benoiton et al and Gaede references would be *literally infringing* on the instantly claimed methods should the instantly claimed methods be patented. The literal definition, as set forth *supra,* of the word "add" shows that no matter what the spatial relationship of one solution to the other before the mixing occurs, if the two are mixed, then one has been added to the other, and *vice versa;* See *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.,* 246 F .3d 1368, 1378 (Fed. Cir. 2001) - ("it is axiomatic that that which would literally infringe if later anticipates if earlier").

Applicant's position is as if to say that if the Examiner were to place cream in his coffee cup first, and *then* pour coffee into the cup, then the Examiner did not add cream to his coffee. This is obviously not the case when it can be seen that the coffee has cream in it, therefore cream has been added to coffee. Applicant's position is tantamount to stating that putting cream in the cup first, and *then* pouring coffee into the cup produces a result entirely different, but the issue is only whether or not the cream and coffee have been combined, to make coffee with cream in it. The instantly claimed methods specify the same result disclosed by the cited prior art.

The claims specify a method comprising adding one thing to another, which produces a certain type of compound. Urbanski et al, Ramage et al, Benoiton et al, and Gaede (as applied to the appropriate claims) disclose adding the same two things together, which adding produces the same compounds.

Second, point #2 is addressed:

A showing of unexpected results is not sufficient to overcome an anticipation rejection. Even if such unexpected results were enough to overcome such a rejection, it should be pointed out that the Examples in the instant specification only demonstrate the synthesis one kind out of the numerous functionally diverse types of mixed anhydrides that can be constructed from the instantly claimed methods. In fact, the Examples disclose the formation of compounds most accurately described as carbonates, not anhydrides. One of ordinary skill in the art would not expect the results gleaned from the synthesis of these carbonates to automatically carry over to all of the many types of mixed (unsymmetrical) anhydrides within the scope of the claimed invention, including but not limited to: carboxylic-carboxylic, carboxylic-phosphoric, carboxylic-sulfonic, carboxylic-phosphinic and carboxylic-sulfinic mixed anhydrides.

Allowable Subject Matter

Claim 20 would be allowable if the rejection under 35 U.S.C. 112, second paragraph, were overcome.

Conclusion

This Office action is non-final due to the new claim rejections under 35 U.S.C. 102(b), based on prior art submitted by Applicant in an Information Disclosure Statement with an accompanying statement under 37 C.F.R. 1.97.

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (703) 305-2050. The examiner can normally be reached

Monday-Friday from 7:00am to 3:30pm. If Attempts to reach the examiner are unsuccessful, the examiner's supervisor, Mukund Shah, can be reached at (703) 308-4716. The fax number for the organization where this application or proceeding is assigned is (703) 308-4556 for regular communications and (703) 308-4242 for after-final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

zt

JOHN M. FORD
PRIMARY EXAMINER
GROUP - ART UNIT 1624